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FAITH (HEALING), HOPE AND CHARITY AT THE FDA: THE POLITICS OF AIDS DRUG TRIALS

GEORGE J. ANNAS*

I. INTRODUCTION

AIDS forces us to confront our mortality, the limits of modern medicine and the contours of our compassion. How we respond is a measure of our society and a reflection of our values and priorities. As a fundamentally death-denying society, our response has been hampered by denial and shaped by faith that a technological fix will make the AIDS epidemic go away. Technology is our new religion, our “modern” way to deal with death. As novelist Don DeLillo has one of his characters put it to another who is worried about death: you can deny it, you can put your faith in religion or

[y]ou [can] put your faith in technology. It got you here, it can get you out. This is the whole point of technology. It creates an appetite for immortality on the one hand. It threatens universal extinction on the other. . . .

It's what we invented to conceal the terrible secret of our decaying bodies. But it's also life, isn't it? It prolongs life, it provides new organs for those that wear out. New devices, new techniques every day. Lasers, masers, ultrasound. Give yourself up to it. . . . They'll insert you in a gleaming tube, irradiate your body with the basic stuff of the universe. Light, energy, dreams. God's own goodness.¹

The less we understand about medical technology, the more we see it as magic. Nor are physicians immune from magical thinking. As psychiatrist Jay Katz has noted, when medical sci-

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1. D. DELILLO, *WHITE NOISE* 285 (1985).

ence seems impotent to fight the claims of nature, "all kinds of senseless interventions are tried in an unconscious effort to cure the incurable magically through a 'wonder drug,' a novel surgical procedure, or a penetrating psychological interpretation."² Katz noted further that although physicians often justify such interventions as simply being responsive to patient needs, "[they] may turn out to be a projection of their own needs onto patients."³ In a parallel fashion, we speak of medical "miracles" in recounting techniques we cannot understand, but nonetheless in which we want to believe. We have become modern believers in faith healing, faith based not in a Supreme Being, but in Supreme Science.

The AIDS epidemic has frightened us into believing that medicine will find a cure soon, and this misplaced faith in science has helped erode the distinction between experimentation and therapy; has threatened to transform the United States Food and Drug Administration (FDA) from a consumer protection agency into a medical technology promotion agency; and has put AIDS patients, already suffering from an incurable disease, at further risk of psychological, physical and financial exploitation by those who would sell them useless drugs. The not-too-subtle metamorphosis of the FDA has been abetted by an unusual political alliance between the anti-regulation Reagan and Bush administrations and gay rights activists.

This article argues that the distinction between experimental and therapeutic interventions is crucial to both science and individual rights, and that the FDA should continue to responsibly regulate experimental drugs and maintain its identity as a premier consumer protection agency. We should not permit the AIDS epidemic to be used as an excuse to dismantle the FDA or to put the integrity of our drugs and medical devices at risk. True compassion for AIDS patients does *not* involve dispensing false hope or unreasonable hype. It requires adequate funding and staffing of the National Institutes of Health's (NIH) AIDS drug and vaccine research and testing programs, and maintaining scientifically sound testing methodologies that can provide reasonable assurance that the drugs that are sold as therapies are safe and effective. To examine the politics of AIDS drug development, it is first necessary to understand the purposes for the experimentation-therapy distinction in medicine and the values that this distinction promotes and protects.

2. J. KATZ, *THE SILENT WORLD OF DOCTOR AND PATIENT* 151 (1984).

3. *Id.*

II. THE DISTINCTION BETWEEN EXPERIMENTATION AND THERAPY

Perhaps the major source of controversy surrounding drug trials for experimental AIDS drugs is that the investigators see these trials as *research* designed to provide generalizable knowledge that may help others,⁴ while most individuals suffering with AIDS see these trials as *therapy* designed to benefit them.⁵ This misconception is not new,⁶ and a glance at the history of human experimentation shows why this difference in perspectives is so important.

A reasonable summary of many of the major issues in human experimentation appears in Gustave Flaubert's realistic novel *Madame Bovary*.⁷ A character in this novel, Charles Bovary, decided to try to make his name as a physician by curing the local stableman's clubfoot with experimental surgery. The experiment involved cutting the Achilles tendon and then screwing the foot and leg into "a sort of box weighing about eight pounds—a complicated mass of iron, wood, tin, leather, screws and nuts,"⁸ which

4. Some commentators object to the research-practice dichotomy, arguing that all therapy has elements of research in it, and much of medical practice involves the use of "nonvalidated practices" or "investigational" procedures that have not been subjected to rigorous research methods. Professor Robert J. Levine probably makes the argument as well as anyone in his standard reference on research with human subjects. See R. LEVINE, *ETHICS AND REGULATION OF CLINICAL RESEARCH* 3-10 (2d ed. 1986). Nonetheless, no matter what terms are employed, the fundamental question remains: when is it reasonable and appropriate to use standard rules regarding research on human beings to protect their interests, and when can these rules be ignored or abandoned altogether? This, of course, is the central question in using "new," "investigational" and "nonvalidated" drugs and treatments on AIDS patients. In this regard, changing the terminology does not help either patients or their providers to determine any better than the research-practice dichotomy does whether special protections are required.

5. Levine, *Has AIDS Changed the Ethics of Human Subjects Research?*, 16 *LAW MED. & HEALTH CARE* 167, 171 (1988). Levine answers the question posed in the title of her article by pointing out the changes AIDS research has made in research ethics. First, the consent of the subject to use certain specimens in research is not always required. *Id.* at 169. Second, subjects are not necessarily informed of their test results. *Id.* at 170. Third, the confidentiality of subjects' identity is often compromised when balanced against "third parties who may be placed at risk by their subjects' behavior." *Id.*

6. *Id.* at 171-72 (quoting Appelbaum, Roth, Lidz *et al.*, *False Hopes and Best Data: Consent to Research and the Therapeutic Misconception*, *HASTINGS CENTER REP.*, Apr. 1987, at 20) (therapeutic misconception is when patient who is also subject feels "that every aspect of the research project to which he had consented was designed to benefit him directly"). Rather than characterize any particular drug as a "research drug" versus a "therapy drug," it is probably more accurate to think of a drug as falling on a continuum from "experimental" to "investigational" to "suspected effective" to "nonvalidated" to "proven effective."

7. G. FLAUBERT, *MADAME BOVARY* (F. Steegmuller trans. 1957).

8. *Id.* at 198.

was constructed by the cabinetmaker and the locksmith. The apothecary, who was an avid promoter of the operation, tried to convince Charles's wife, Emma, of the operation's merits by asking her:

"After all, . . . what's the risk? Look." And he enumerated on his fingers the advantages that would accrue from the attempt. "Almost sure success, relief and improved appearance for the patient, and for the surgeon a rapid rise to fame. Why shouldn't your husband fix up poor Hippolyte?"⁹

The entire town urged the stableman to consent but "what finally decided him was that it *wouldn't cost him anything*."¹⁰ The experiment did not go as planned and another physician eventually was called to amputate the hideously painful and gangrenous leg.¹¹ Most experiments do not have such disastrous results for patients; but many share similar dangers, as well as the same motivations on the part of both physician and patient, the same inability to separate hope from realistic appraisal of likely outcomes and the same inability to distinguish voluntary consent from coercion. To protect subjects, rules have been developed regarding human experimentation.

The most comprehensive and authoritative legal statement on human experimentation is embodied in the ten-point Nuremberg Code, articulated in a court opinion following the trial of Nazi physicians for "war crimes and crimes against humanity" committed during World War II.¹² These crimes included human experiments designed to determine which poisons killed the fastest, how long people could live when exposed to ice water and when exposed to high altitudes, and whether surgically severed limbs could be reattached.¹³ The Nuremberg tribunal rejected the defendants' contention that their experiments on both prisoners of war and civilians were consistent with the ethics of the medical profession as evidenced by previously published American, French and British experiments on venereal disease, plague, and

9. *Id.* at 196.

10. *Id.* at 198 (emphasis added).

11. *Id.* at 207.

12. 2 TRIALS OF WAR CRIMINALS BEFORE THE NUERNBERG MILITARY TRIBUNALS UNDER CONTROL COUNCIL LAW NO. 10 181-82 (1949) [hereinafter NUERNBERG TRIALS].

13. 1 NUERNBERG TRIALS, *supra* note 12, at 11-14.

malaria, and by American prison experiments, among others.¹⁴ The tribunal concluded that only “certain types of medical experiments on human beings, when *kept within reasonably well-defined bounds*, conform to the ethics of the medical profession generally.”¹⁵

These well-defined bounds are articulated in the ten principles which make up the Nuremberg Code. The basis of the Code is a type of natural law reasoning. In the tribunal’s words: “All agree . . . that certain basic principles must be observed in order to satisfy moral, ethical and legal concepts.”¹⁶ Principle 1 of the Nuremberg Code requires that the consent of the experimental subject have at least four characteristics: it must be competent, voluntary, informed and comprehending.¹⁷ This is to protect the subject’s rights.

The other nine principles have to do primarily with protecting the subject’s welfare: they prescribe actions that must be taken *prior* to seeking subject enrollment in the experiment and actions that must be taken to protect the subject during the experiment. These include a determination that the experiment is properly designed to yield fruitful results “unprocurable by other methods”; that “anticipated results” will justify performance of the experiment; that all “unnecessary physical and mental suffering and injury” is avoided; that there is no “*a priori* reason to believe that death or disabling injury will occur”; that the project

14. 2 NUERNBERG TRIALS, *supra* note 12, at 92-93.

15. *Id.* at 181 (emphasis added).

16. *Id.*

17. *Id.* at 181-82. The first basic principle laid down by the judges was: The voluntary consent of the human subject is absolutely essential.

This means that the person involved should have *legal capacity to give consent*; should be so situated as to be able to exercise *free power of choice*, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have *sufficient knowledge and comprehension* of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

Id. (emphasis added).

has "humanitarian importance" that outweighs the degree of risk; that adequate preparation is taken to "protect the experimental subject against even remote possibilities of injury, disability, or death"; that only "scientifically qualified" persons conduct the experiment; that the subject can terminate participation at any time; and that the experimenter is prepared to terminate the experiment if "continuation of the experiment is likely to result in injury, disability, or death to the experimental subject."¹⁸ The Code has been used as the basis for other international documents such as the Declaration of Helsinki. It is a part of international common law, and I have previously argued that it can properly be viewed as both a criminal and civil basis for liability in the United States.¹⁹

18. *Id.* at 182.

19. G. ANNAS, L. GLANTZ & B. KATZ, *INFORMED CONSENT TO HUMAN EXPERIMENTATION: THE SUBJECT'S DILEMMA* 21 (1977). Surprisingly, when the United States Supreme Court had a chance to adopt and endorse the principles of the Nuremberg Code in 1987, it failed to recognize the Code as binding upon the United States military. *United States v. Stanley*, 483 U.S. 669 (1987) (5-to-4 decision).

Stanley involved a lawsuit brought by an Army serviceman who, while in the service, had been secretly given LSD in 1958 to determine its effects. The LSD caused Stanley to suffer from hallucinations, periods of incoherence and memory loss and to awaken in the middle of the night and violently beat his wife and children. He was discharged from the Army in 1969 and divorced shortly thereafter because of the LSD-induced personality changes. In 1975, the Army sent him a letter asking him to cooperate in a follow-up study on the long-term effects of LSD on "volunteers who participated" in the 1958 tests. This was the first he learned of the experiment. *Id.* at 672. When his suit reached the United States Supreme Court, the majority of the Court concluded that involuntary participation in human experimentation was no exception to the rule that a serviceman could not sue the federal government for injuries which "arise out of or are in the course of activity incident to service." *Id.* at 684.

The four dissenting Justices based their disapproval of this conclusion primarily on the principles enunciated in the Nuremberg Code. Justice William Brennan, writing in dissent, pointed out that it was "[t]he United States military [who] developed the Code, which applies to all citizens—soldiers as well as civilians." *Id.* at 687 (Brennan, J., dissenting). Justice Brennan went on to note that in addition to the thousands of soldiers and civilians who have been subjected to secret LSD experiments by the government, an estimated 250,000 military personnel were exposed to large doses of radiation between 1945 and 1963 while engaged in maneuvers designed to determine the effectiveness of combat troops in nuclear battlefield conditions. Explaining why the Nuremberg Code and the principle of voluntary consent for which it stands must apply to the military as well as civilians, Justice Brennan stated that "[t]he subject of experimentation who has not volunteered is treated as an object, a sample. . . . Soldiers ought not be asked to defend a Constitution indifferent to their essential human dignity." *Id.* at 708 (Brennan, J., dissenting).

This decision is a disgrace. The Nuremberg Code should be seen as setting a *minimal* legal standard for licit human experimentation, both in and out of the military. See generally R. LIFTON, *THE NAZI DOCTORS: MEDICAL KILLING AND THE PSYCHOLOGY OF GENOCIDE* 503 (1986) (Nazi genocide began with doctors killing

Today the most likely subject of medical experimentation is not the prisoner or even the soldier, but the patient with a disease. As a leading medical commentator has stated:

Volunteers for experiments will usually be influenced by hopes of obtaining better grades, earlier parole, more substantial egos, or just mundane cash. These pressures, however, are but fractional shadows of those enclosing the patient-subject. *Incapacitated and hospitalized because of illness, frightened by strange and impersonal routines, and fearful for his health and perhaps life, he is far from exercising a free power of choice* when the person to whom he anchors all his hopes asks, "Say, you wouldn't mind, would you, if you joined some of the other patients on this floor and helped us to carry out some very important research we are doing?" When "informed consent" is obtained, it is not the student, the destitute bum, or the prisoner to whom, by virtue of his condition, the thumb screws of coercion are most relentlessly applied; it is *the most used and useful of all experimental subjects, the patient with disease*.²⁰

When the illness is fatal, pressures on both the physician-researcher and patient are much more acute, and the rules regarding research seem less relevant. Consent also seems a sham since patients are desperate and *demand* to be research subjects thinking that this is their best hope of getting treatment for their condition. The assertion is made that patients have "nothing to lose" by engaging in all manner of experimentation and that patients should have the "right" to be experimental subjects.²¹ But it is when such political claims are made in the face of a fatal disease

in name of healing); Bassiouni, Baffes & Evrard, *An Appraisal of Human Experimentation in International Law and Practice: The Need for International Regulation of Human Experimentation*, 72 J. CRIM. L. & CRIMINOLOGY 1957, 1642 (1981) (human experimentation is necessary for development of modern medicine and science, but there needs to be international code establishing clear definition of human experimentation and boundaries to its lawfulness and unlawfulness).

20. Ingelfinger, *Informed (But Uneducated) Consent*, 287 NEW ENG. J. MED. 465, 466 (1972) (emphasis added).

21. A French AIDS researcher experimenting with HPA-23 said of AIDS patients in 1984: "What do these people have to lose?" R. SHILTS, AND THE BAND PLAYED ON 496 (1987). Even their advocates echo this rhetoric. See, e.g., L. KRAMER, REPORTS FROM THE HOLOCAUST 142 (1989) ("AIDS sufferers, who have nothing to lose, are more than willing to be guinea pigs."). Similar statements were made by physicians using experimental artificial hearts at about the same time. Annas, *The Phoenix Heart: What We Have to Lose*, HASTINGS CENTER REP., June 1985, at 15.

that consumer protection agencies like the FDA must stand firm and insist on the scientific validity of those experiments. This is because, as important as informed consent is, the first and most important question is whether the experiment should be done at all.²² Only after this determination has been made, based on factors such as prior animal and laboratory research, study design, risk/benefit analysis and a consideration of the alternatives, is it even legitimate to ask the subject to participate.²³ Without such prior determinations and the development of a sound research protocol, it is extremely unlikely that experimentation will yield any useful information, but rather will serve only to increase the suffering and exploitation of desperate patients.

III. THE POLITICS OF AIDS DRUG TRIALS

The politics of AIDS has produced strange political alliances. The anti-regulation Reagan and Bush administrations and the gay community probably have only one interest in common: deregulating the drug approval process.²⁴ The gay community's position is probably best summed up in a slogan used by ACT-UP (AIDS Coalition to Unleash Power): "A Drug Trial is Health Care Too."²⁵ The truth is otherwise: a drug trial is research designed to test a hypothesis, not to help individual patients. The reason for this strange alliance has little to do with shared love for those suffering with AIDS, but rather is attributable to administrations composed largely of free market advocates and the deregulation

22. Fletcher, *The Evolution of the Ethics of Informed Consent*, in RESEARCH ETHICS 211 (K. Berg & K. Tranoy eds. 1983).

23. G. ANNAS, THE RIGHTS OF PATIENTS 142 (2d ed. 1989). AIDS drug development has been significantly hampered by lack of an animal that can be infected with HIV. Chimpanzees can be infected, but do not become sick. They are also an endangered species. Recently, two mice models have been developed which should provide an animal model in which to test potential AIDS drugs prior to conducting human trials. For a discussion of the two mice models, see Leonard, Abramczuk, Pezen *et al.*, *Development of Disease and Virus Recovery in Transgenic Mice Containing HIV Proviral DNA*, 242 SCI. 1665 (1988); Namikawa, Kaneshima, Lieberman & McCune, *Infection of the SCID-hu Mouse by HIV-1*, 242 SCI. 1684 (1988).

24. Kolata, *Odd Alliance Would Speed New Drugs*, N.Y. Times, Nov. 26, 1988, at 9, col. 4. As one AIDS lawyer commented: "It's a very curious situation . . . [w]hen you find yourself in a position of articulating positions that are also being put forth by the Competitive Enterprise Institute or the Heritage Foundation, this is really bizarre." *Id.*

25. *Why AIDS Activists Target the FDA*, Village Voice, Oct. 18, 1988, at 25, col. 1. See also *Mainstream Strategy for AIDS Group*, N.Y. Times, July 22, 1988, at B1, col. 2, B4, col. 6 (ACT-UP is also involved "in extensive research to find promising experimental drugs and treatment programs, and monitor progress in drug trials").

lobbying of drug companies which see the AIDS epidemic as an opportunity to further their own interests.

Unlike the treatment in *Madame Bovary*, research drugs are no longer universally delivered free, and there is tremendous pressure on the FDA to permit drug companies to sell "promising" experimental drugs to subjects. The sale of experimental drugs threatens to further erode the distinction between experimentation and therapy, and makes it even more difficult for patients suffering from disease to distinguish recognized therapy from early experimentation, and false hope from reasonable expectation.

The administration's position is that drugs should be permitted to go on the market faster. President George Bush, while still Vice-President, urged the FDA to develop procedures to expedite the marketing of new drugs intended to treat AIDS and other life-threatening illnesses.²⁶ In his first debate with the Democratic nominee, Michael Dukakis, President Bush said that in response to his efforts the FDA had "sped up bringing drugs to market that can help."²⁷ However, the President did caution that "you've got to be careful here because there's a safety factor."²⁸ Indeed there should be a safety factor, and the policy question is whether it should be ignored or radically lessened when the research subjects have a fatal illness for which there is no cure. Although the AIDS epidemic is new, this question is not. The FDA has faced it squarely before.

In the 1970s, thousands of cancer victims were traveling to Mexico and Canada to obtain laetrile, a substance derived from apricot pits. The drug was not available in the United States and was not even in experimental trials. In 1975, a group of terminally ill cancer patients and their spouses sued the federal government to enjoin it from interfering with the interstate shipment and sale of laetrile.²⁹ The FDA vigorously opposed making lae-

26. Investigational New Drug, Antibiotic and Biological Drug Product Regulations; Procedures for Drugs Intended to Treat Life-Threatening and Severely Debilitating Illnesses; Interim Rule, 53 Fed. Reg. 41,515, 41,516 (1988) (to be codified at 21 C.F.R. §§ 312, 314) [hereinafter *Investigational New Drug Regulations*]. See also Leary, *Panel Seeks to Streamline F.D.A. for Cancer and AIDS Drugs*, N.Y. Times, Jan. 5, 1989, at B12, col. 2 (panel of experts established at request of President Bush is trying to find ways to speed approval process of drugs to treat AIDS and cancer).

27. *Transcript of the First TV Debate Between Bush and Dukakis*, N.Y. Times, Sept. 26, 1988, at A16, col. 1.

28. *Id.*

29. *United States v. Rutherford*, 442 U.S. 544 (1979).

trile available in the United States, even to terminally ill cancer patients, because "there were no adequate well-controlled scientific studies of Laetrile's safety or effectiveness."³⁰

The United States Supreme Court in *United States v. Rutherford*³¹ upheld the FDA's position, noting, among other things, that "[i]n implementing the statutory scheme, the FDA has never made exception for drugs used by the terminally ill."³² The Court also agreed with the FDA that effectiveness is not irrelevant simply because a person is dying. The *Rutherford* Court stated: "[E]ffectiveness does not necessarily denote capacity to cure. In the treatment of any illness, terminal or otherwise, a drug is effective if it fulfills, by objective indices, its sponsor's claims of prolonged life, improved physical condition, or reduced pain."³³ The Court reasoned that safety is also relevant to the terminally ill, stating that "[f]or the terminally ill, as for anyone else, a drug is unsafe if its potential for inflicting death or physical injury is not offset by the possibility of therapeutic benefit."³⁴ The Court emphasized that although the case involved laetrile, the logic adopted applied to all unproven drugs:

To accept the proposition that the safety and efficacy standards of the Act have no relevance for terminal patients is to deny the Commissioner's authority over all drugs, however toxic or ineffectual, for such individuals. If history is any guide, this new market would not be long overlooked. Since the turn of the century, resourceful entrepreneurs have advertised a wide variety of purportedly simple and painless cures for cancer, including liniments of turpentine, mustard, oil, eggs, and ammonia; peat moss; arrangements of colored flood-lamps; pastes made from glycerin and limburger cheese; mineral tablets; and "Fountain of Youth" mixtures of spices, oil, and suet. . . . Congress could reasonably have determined to protect the terminally ill, no less than other patients, from the vast range of self-styled pan-

30. *Id.* at 549. Laetrile's advocates accused the government of suppressing a "cure" for cancer and of murdering cancer victims in their own experiments. The basic arguments now being made by AIDS activists are the same that were previously made by laetrile activists. See, e.g., G. GRIFFIN, *WORLD WITHOUT CANCER: THE STORY OF VITAMIN B17* (1974).

31. 442 U.S. 544 (1979).

32. *Id.* at 553.

33. *Id.* at 555.

34. *Id.* at 555-56.

aceas that inventive minds can devise.³⁵

Since 1979, the FDA's public position on the use of unproven drugs and devices in clinical settings has shifted. In 1985, for example, the FDA decided to encourage the use of temporary artificial hearts, even though their use in clinical settings outside of a planned research project could generate no scientifically useful information about these devices.³⁶ The justification was that the FDA should not stand in the way of a physician using an unapproved medical device in an "emergency."³⁷ In 1987, in response to increasing political pressure to make experimental AIDS drugs more widely available, the FDA issued new regulations that permit the treatment use and sale of an investigational new drug (IND) that is not otherwise approved for treatment and sale, while the drug is still in clinical trials, if:

- (i) The drug is intended to treat a serious or immediately life-threatening disease;
- (ii) There is no comparable or satisfactory alternative drug or other therapy available to treat that stage of the disease in the intended patient population;
- (iii) The drug is under investigation in a controlled clinical trial under an IND in effect for the trial, or all clinical trials have been completed; and
- (iv) The sponsor of the controlled clinical trial is ac-

35. *Id.* at 557-58. The illusion that cancer can be cured by simply dedicating money and resources to this task, first proposed by Richard Nixon in his "war on cancer," remains alive today. See Hammer, *Funds are Lacking, Cancer is Gaining*, N.Y. Times, Jan. 16, 1989, at A17, col. 3.

36. Annas, *Death and the Magic Machine: Informed Consent to the Artificial Heart*, 9 W. NEW ENG. L. REV. 89, 107 (1987). See also Copeland, Levinson, Smith *et al.*, *The Total Artificial Heart as a Bridge to Transplantation: A Report of Two Cases*, 256 J. A.M.A. 2991, 2991 (1986) (These researchers' first attempt at using an artificial heart as a "bridge" was with unapproved device.).

37. Annas, *supra* note 36, at 108. See also *The Man with the Illegal Heart*, N.Y. Times, Mar. 9, 1985, at 22, col. 1 (FDA regulates experimental medical devices but artificial heart can be considered emergency treatment); Guidance for the Emergency Use of Unapproved Medical Devices, Availability, 50 Fed. Reg. 42,865 (1985) (FDA does not object to use of unapproved potentially life-saving medical device in emergency). The FDA established three preconditions for a situation to be considered an emergency:

- 1. The patient is in a life-threatening condition that needs immediate treatment;
- 2. No generally acceptable alternative for treating the patient is available; and
- 3. Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

Id. at 42,867.

tively pursuing marketing approval of the investigational drug with due diligence.³⁸

According to the counselor to the Undersecretary of Health and Human Services, S. Jay Plager, the purpose of these new rules is to give "'desperately ill patients' the opportunity to decide for themselves 'whether they would rather take an experimental drug or die of the disease untreated.'"³⁹ Like ACT-UP, Mr. Plager and the FDA confuse experimentation with treatment and seem so intent on denying death that they believe it can be magically prevented with unproven drugs.

No one opposes cutting "red tape" or removing regulatory hurdles that do not improve safety and efficacy. Arguably, the FDA's rules are not inconsistent with *Rutherford*.⁴⁰ But the FDA

38. Treatment Use of an Investigational New Drug, 21 C.F.R. § 312.34 (1988). See Young, Norris, Levitt & Nightingale, *The FDA's New Procedures for the Use of Investigational Drugs in Treatment*, 259 J. A.M.A. 2267, 2268 (1988).

39. Pear, *U.S. to Allow Use of Trial Drugs for AIDS and Other Terminal Ills*, N.Y. Times, May 21, 1987, at A1, col. 5. A year later these new rules were termed a "failure" by the President's AIDS Commission which identified four reasons for their nonuse:

[S]ome pharmaceutical companies are unwilling to allow their drugs to be used in this program, even when they are sought after by physicians and desperately ill patients; there is no information system that allows the patient or physician population to know what is available; methods of obtaining drugs that are available through this program are poorly understood and seem unnecessarily complicated; and some physicians are reluctant to prescribe treatment IND drugs because liability limits are not clearly defined.

REPORT OF THE PRESIDENTIAL COMMISSION ON THE HUMAN IMMUNODEFICIENCY VIRUS EPIDEMIC 50 (1988). As the Commission noted, in the first year of the new rules, only one sponsor applied for and obtained approval for a treatment IND for an HIV-related product. *Id.* See also Boffey, *New Initiative to Speed AIDS Drugs Is Assailed*, N.Y. Times, July 5, 1988, at C1, col. 1, C9, col. 1 (AIDS commission described new program as "a failure because it had not produced drugs to attack the AIDS virus directly").

40. The FDA provided the following explanation of why the new rules did not conflict with *Rutherford*:

In *Rutherford*, the Court held that the new drug approval requirements of the act applied to drugs intended to treat persons with terminal diseases and upheld FDA's determination that Laetrile was an unapproved new drug that could not be shipped in interstate commerce. However, the treatment IND/protocol and sale provisions of the final rule are not inconsistent with *Rutherford*. The Court in *Rutherford* noted that application of the new drug approval provisions to therapies for terminal diseases did not foreclose resort to experimental drugs by patients for whom conventional therapy was unavailable. The Court noted that the act makes explicit provision for carefully regulated use of certain drugs not yet demonstrated safe and effective. The final rule, while permitting cost recovery for certain investigational drugs, maintains the prohibition against commercialization; distribution of a drug under an

Commissioner took a step that clearly is inconsistent when, in July 1988, he announced that the FDA would permit United States citizens to import unapproved drugs from abroad for their personal use.⁴¹ In attempting to justify this policy, Commissioner Frank Young said that “[t]here is such a degree of desperation, and people are going to die, that I’m not going to be the Commissioner that robs them of hope.”⁴² The reaction of the scientific community to this new FDA position was well summed up in an article in *Science*: “The new directive stunned some AIDS researchers. One official in the federal government’s AIDS Program went so far as to suggest that the FDA commissioner had gone ‘temporarily insane.’”⁴³ There are at least three reasons for this reaction.

First are all the arguments the FDA used in *Rutherford* to justify its central role as a consumer protection agency. All patients, particularly terminally ill patients, deserve protection from profit seekers who want to prey on their desperation.⁴⁴ People with AIDS have a lot to lose, including their health, lives, dignity and money. They can be and have been viciously exploited. Because many victims of AIDS are members of disenfranchised groups that have traditionally been rightfully suspicious of government’s view of them, they may be at special risk for exploitation by those who proclaim that the government and orthodox medicine are in

approved treatment IND/protocol, therefore, continues to be a carefully regulated distribution. Treatment use of an investigational drug is conditioned on the sponsor complying with all the safeguards inherent in the IND process including informed consent, IRB review and the applicable provisions of Part 312, such as distribution of the drug through qualified experts, maintenance of adequate manufacturing facilities, and submission of IND safety reports. The treatment IND/protocol provisions and the provisions for cost recovery, operating together, are consistent with the Court’s opinion in *Rutherford*.

52 Fed. Reg. 19,465, 19,473 (1987) (citations omitted). For a discussion of *Rutherford*, see *supra* notes 29-35 and accompanying text.

41. Boffey, *FDA Will Allow AIDS Patients to Import Unapproved Medicines*, N.Y. Times, July 24, 1988, at 1, col. 1. Up to three months supply can be imported, and a physician’s name must be given. *Id.*

42. *Id.*

43. Booth, *An Underground Drug for AIDS*, 249 SCIENCE 1279 (1988). Donald Abrams, an AIDS researcher at San Francisco General Hospital, commented that “[t]he FDA is saying: ‘We can’t regulate anymore. So who cares? Let the patients take whatever they want! Just get them off our backs.’” *Id.*

44. Approximately \$1 billion is now being spent annually on bogus AIDS treatments in the United States alone. There are hundreds of quack doctors peddling half-truths, false hopes and potentially lethal treatments. In the words of John Renner of the National Council Against Health Fraud, “[t]here is an entire world of mischief and hucksterism out there . . . spreading disinformation, panic and fear.” Manmaney, Quan, Ard & Wright, *Preying on AIDS Patients*, NEWSWEEK, June 1, 1987, at 52.

a conspiracy to deny them treatment.⁴⁵

A few examples of harm to individuals from unapproved drugs illustrate the problem. The life and death of Bill Kraus frames Randy Shilts' chronicle of the politics of AIDS, *And The Band Played On*.⁴⁶ Kraus, like many other AIDS patients, including Rock Hudson (who left Paris in 1984 convinced he was cured of AIDS), traveled to Paris to be treated with HPA-23. When, in 1985, it became clear that the drug was not working, Kraus' doctor urged him to start taking isoprinosine, another unproven medication. Shilts writes: "The suggestion upset Bill because he had pinned his entire hope for survival on HPA-23. Even the possibility that it might not be a panacea enraged him, cutting to the core of his denial and bargaining with his AIDS diagnosis."⁴⁷ More than five years later, the efficacy of HPA-23 is still in doubt, and obviously the failure to prove or disprove its worth in France cannot be blamed on the FDA's regulations.

Suramin, which has been widely used to treat African sleeping sickness, was discovered to disable HIV's ability to replicate in the test tube. When the test tube information was made public

45. See J. YOUNG, *THE MEDICAL MESSIAHS: A SOCIAL HISTORY OF HEALTH QUACKERY IN TWENTIETH-CENTURY AMERICA* 428 (1967). Professor Young explores the reasons why people subscribe to quack remedies and states:

The poorly educated do after all pay most of the bills. Among them is a group motivated, it would seem, by something more than sheer lack of knowledge. Some sort of alienation, some sort of perversity, drives these people to follow the most extreme pathways. Often they share with others not so far out as themselves a deep resentment against orthodox authority.

Id.

46. R. SHILTS, *supra* note 21.

47. *Id.* at 562. Shilts notes that "[a]bout 100 Americans were part of the AIDS exile community in Paris, making long daily treks to Percy Hospital on the edge of the city for their shots of HPA-23." *Id.* at 563. Shilts also notes that as early as 1983 the amino acid clinics in Mexico were making

a killing from desperate AIDS victims seeking a reprieve from their death sentences. The fact that you had to leave the country for treatments rejected by the medical establishment only made them seem all the more tantalizing. Patients recently diagnosed with a fatal illness tended not to be wild about anything that smacked of official medicine.

Id. at 240-41.

Others are beginning to tell similar stories. Chris Clason, founder of the Test Positive Aware support group in Chicago, says:

People get all jazzed up about the next drug to come down the chute, do whatever they need to do to get it, and then find out a couple of years later that it's not very appropriate or effective. . . . Then they get depressed and wish they hadn't sold the condo . . . [but when the next drug comes along] they jump back on the roller coaster.

Cotton, *Easing Import Difficulties Hasn't Provided Panacea*, Med. World News, Apr. 10, 1989, at 36, col. 3.

and the drug touted as “promising,” many patients wanted it. However, a subsequent trial in humans found that the drug was extremely toxic in AIDS patients, worsening immune disorders and thus hastening death.⁴⁸ French researchers announced to the world that they had cured AIDS using cyclosporine.⁴⁹ There was a clamor for the drug, and the announcement was later found to be premature hype when both patients became comatose and the drug did not improve their clinical course. In late 1987, a Zairian scientist announced in a news conference that he had a possible cure for AIDS. In the aftermath of the announcement, the number of men in Zaire who believed AIDS could be cured doubled to fifty-seven percent and educational efforts aimed at prevention were set back.⁵⁰

The lack of scientifically sound, carefully planned, randomized clinical trials not only produces false hope, but can also directly lengthen the time it will take to get a truly effective AIDS drug to those suffering from the disease. One of the most promising AIDS drugs, amplitgen, had been backed for clinical testing by Du Pont, which had committed as much as \$25 million to its study. In October 1988, the trials were halted when it appeared to do no better than a placebo. However, in January 1989, its primary developer announced that it thought the drug had been prematurely abandoned, saying that the poor results could be attributed to the haste in which the relatively large batch of the drug was manufactured and shipped over long distances. New trials may start later in 1989.⁵¹

48. Eckholm, *Should the Rules Be Bent in an Epidemic?*, N.Y. Times, July 13, 1986, at E30, col. 1; See also Levy, *Ethical Dilemma of Placebo-Controlled Trials in Life-Threatening Illnesses*, 2 J. CLINICAL RES. & DRUG DEV. 145, 151 (1988) (reviews basic principles of ethical clinical research design for experimental treatment of life-threatening illnesses and applies them to AZT context).

49. Clark, Lerner & Stadtman, *AIDS: A 'Breakthrough'?*, NEWSWEEK, Nov. 11, 1985, at 88.

50. Brooke, *In Zaire, AIDS Awareness vs. Prevention*, N.Y. Times, Oct. 10, 1988, at B4, col. 1.

51. Andrews, *3 New Drugs Backed for AIDS Study*, N.Y. Times, Jan. 7, 1989, at 36, col. 1. See Hays, *Du Pont's Big Drive To Enter Drug Field Proves Disappointing*, Wall St. J., Jan. 16, 1989, at A1, col. 6. The amplitgen story has become even more complex as details of charges and countercharges appear in the press. The rights to amplitgen were held by a small, private biotechnology firm in Philadelphia, Pennsylvania, called HEM Research Inc. *Id.* at A10, col. 2. One of the drug's developers, and chairman of the company, had sought out Du Pont as a partner to develop the drug. *Id.* Although the drug had been tried on only 10 patients (whose immune systems it seemed to stabilize without serious side effects), Du Pont nonetheless agreed to become a partner, acquiring six percent of HEM's stock for \$10 million and agreeing to finance part of a 300 person clinical trial of amplitgen. *Id.* at A10, col. 3. In retrospect, after the failure of the trials,

The second reason why encouraging the use of unproven drugs is bad public policy is that denying death ultimately serves no purpose (other than providing temporary false reassurance). The FDA and other federal agencies (like the Centers for Disease Control) have recognized this in other aspects of the AIDS epidemic. For example, rather than continue to deny that teenagers are engaging in sexual activity, condom use and "safe sex" practices have been recommended to help prevent the spread of AIDS. Similarly, education about the science and epidemiology of AIDS has been used as the major weapon to fight fear and prejudice against those infected by others who would deny them education, housing, employment and insurance.⁵² The scientific facts have been seen as the most powerful weapon against fear bred by ignorance. It is thus at least ironic that attention to scientific facts seems to have been jettisoned when it has come to research with AIDS drugs. It is not compassionate to hold out false hope to terminally ill patients so that they spend their last dollar on unproven "remedies" that they might live longer. If anything, such a strategy seems aimed primarily at treating the guilt of a society that has done little to meet the real needs of AIDS victims by giving us the illusion that we are doing something to help.

The third reason why making unproven drugs available is poor public policy is that if unproven remedies are made easily available it will be impossible to do scientifically valid trials of new drugs. Those suffering from AIDS will be unwilling to participate in randomized clinical trials, and those who are randomized to an

the Du Pont manager in charge conceded the experience was "a good lesson for anybody in this business that early data from uncontrolled studies in small numbers of people can be very misleading." *Id.* HEM's chief executive has since been fired, and in a lawsuit which he filed over his dismissal, the company has counterclaimed, alleging that the former chief executive not only improperly designed the drug trials, but also that he sold HEM stock valued at approximately \$70,000 to a desperate AIDS patient for \$1,000,000 so that the AIDS patient and his friend would be added to the ampligen clinical trial. *Id.* at A1, col. 1, A10, col. 3. HEM alleges that the \$1 million was deposited in the former chairman's personal bank account. *Id.* at A10, col. 3. The former chairman's attorney does not deny the facts, but says "[t]he complaint is an exercise in taking certain facts and matters which individually are correct and reorganizing them or omitting them to leave one with the incorrect impressions." *Id.* See also Iolata, *Poor Results Bring End to Anti-AIDS Drug Study*, N.Y. Times, Oct. 14, 1988, at A13, col. 1 ("People carrying the virus who took ampligen developed AIDS at least as often as patients taking an inert substance.").

52. For a discussion of the use of education about the scientific facts of AIDS to combat fear and discrimination, see R. BAYER, *PRIVATE ACTS, SOCIAL CONSEQUENCES: AIDS AND THE POLITICS OF PUBLIC HEALTH* (1989); AIDS AND THE LAW: A GUIDE FOR THE PUBLIC (H. Dalton, S. Burris & the Yale AIDS Law Project eds. 1987).

arm of the study they do not like will take the drugs they “believe in” on the sly, making any valid finding from the study impossible.⁵³

More recently, in what gay rights activists described as a political ploy in the midst of a presidential campaign, the FDA developed rules designed to permit the collapsing of phases II and III⁵⁴ for certain drugs “intended to treat . . . life-threatening or severely-debilitating illnesses.”⁵⁵ In announcing the new rules, Commissioner Frank Young said: “I’ve seen a lot of folks who are suffering, and I want those people who have either cancer or AIDS to know that this agency has a heart as well as a mind.”⁵⁶ However, these new rules do little more than formalize proce-

53. See, e.g., Kolata, *Recruiting Problems in New York Slowing U.S. Trials of AIDS Drug*, N.Y. Times, Dec. 18, 1988, at 1, col. 4. Not only is there a problem in recruiting AIDS patients to participate in drug trials, but there is the additional problem that those who do join studies may continue to take other “underground” drugs on the side, thus invalidating the results of the study. *Id.* at 46, col. 1. Nonetheless, as of January 1, 1989, there were 5,531 patients enrolled in 57 National Institute of Allergy and Infectious Diseases AIDS protocols across the country. Staver, *HIV-Infected Patients Turn to Aerosol Pentamidine*, Am. Med. News, Jan. 6, 1989, at 11, col. 2. At least one organization, New York’s People with AIDS Health Group, will help AIDS patients import the drugs they want. Kolata, *Group Will Import Unapproved Drugs for Treating AIDS*, N.Y. Times, Mar. 6, 1989, at 1, col. 5.

54. For a discussion of the three phases of human testing to determine if a drug is safe and effective, see Investigational New Drug Regulations, *supra* note 26, at 41,518. The three phases are:

Phase 1 with 10 to 50 patients to study how the drug is tolerated, metabolized, and excreted; phase 2 with 50 to 200 patients in which the safety and efficacy of the drug are first evaluated in controlled trials; and phase 3 with 200 to 1,000 or more patients to confirm and expand upon the safety and efficacy data obtained from the first two phases.

Id. The new rules are premised on the principle that “[i]f . . . the evidence obtained from well-planned and well-executed phase 2 research is sufficient under the statute for marketing approval, there may be no need for additional phase 3 premarket testing, and the drug can become available much more rapidly than usual.” *Id.* at 41,519. For general discussion of the FDA’s drug rules, see Kessler, *The Regulation of Investigational Drugs*, 320 NEW ENG. J. MED. 281 (1989).

55. Investigational New Drug Regulations, *supra* note 26, at 41,516. While some AIDS activists condemned the new rules as mere windowdressing in the midst of the presidential campaign, others, like Barry Gingell of the Gay Men’s Health Crisis, argued that the new rules should be *mandatory* with respect to drug companies, forcing them to cooperate with the FDA to get experimental drugs in the hands of treating physicians as soon as possible. In his words, “I think its [sic] crazy this program is voluntary. . . . Companies should be required by law to design streamlined studies.” Waldholz, *Drug Firms Hope FDA Broadens Plan to Speed Approval of Some Medicines*, Wall St. J., Oct. 21, 1988, at B3, cols. 3, 4.

56. Silver, *FDA Offers Plan to Speed Process of Drug Approval*, Boston Globe, Oct. 20, 1988, at 3, col. 1. This maneuver reportedly led President Bush to decide to keep Young on as FDA Commissioner. Mahar, *Pitiless Scourge: Separating Out the Hype from Hope on AIDS*, BARRON’S, Mar. 13, 1989, at 6, 22.

dures the FDA has always been able to use upon the request of the manufacturer. As the FDA notes in the comments to the rules, they essentially track the way the FDA actually went about approving AZT, still the only drug the FDA has approved for the treatment of AIDS.⁵⁷

57. Investigational New Drug Regulations, *supra* note 26, at 41,519. However, the approval process for azidothymidine (AZT) remains problematic, and we will probably never be able to determine just how effective this drug is for most people suffering from AIDS. This is because the only randomized clinical trial of AZT was terminated before it could be completed because it was found that while only one person receiving AZT had died, 19 on the placebo arm had died. The study involved 282 AIDS patients who either had *Pneumocystis carinii* pneumonia alone or had advanced AIDS-related complex (ARC). They were randomized to AZT or placebo, each taken every four hours, 24 hours a day. Treatment was to last 24 weeks, but when the study was terminated, only 27 subjects had completed the entire 24 weeks of treatment. The researchers concluded that AZT could prolong survival in this patient population, but that "[f]urther studies will be needed to define the optimal dose of AZT and to understand the full range of benefit in the various stages of HIV infection." Fischl, Richman, Grieco *et al.*, *The Efficacy of Azidothymidine (AZT) in the Treatment of Patients with AIDS and AIDS-Related Complex*, 317 NEW ENG. J. MED. 185, 191 (1987) [hereinafter *The Efficacy of AZT*].

AZT, however, is not without adverse side effects, and 21% of AZT recipients in this study developed such severe bone marrow suppression that they required multiple transfusions and had to be discontinued from the drug. Richman, Fischl, Grieco *et al.*, *The Toxicity of Azidothymidine (AZT) in the Treatment of Patients with AIDS and AIDS-Related Complex*, 317 NEW ENG. J. MED. 192, 194 (1987) [hereinafter *The Toxicity of AZT*]. Approving AZT for treatment on the strength of this very limited randomized clinical trial (RCT) has made it difficult to accurately determine AZT's actual effects although it does seem to prolong survival. Creagh-Kirk, Doi, Andrews *et al.*, *Survival Experience Among Patients with AIDS Receiving Zidovudine: Followup of Patients in a Compassionate Plea Program*, 260 J. A.M.A. 3009, 3010 (1988) [hereinafter *Survival Experience*]. Forty percent of those taking AZT, however, develop anemia requiring dose reduction or transfusion, and only 60% of all patients are able to tolerate AZT for more than one year. Bartlett, *HIV Therapeutics: An Emerging Science*, 260 J. A.M.A. 3051, 3051 (1988). See also Schmitt, Bigley, McKinnis *et al.*, *Neuropsychological Outcome of Zidovudine (AZT) Treatment of Patients with AIDS and AIDS-Related Complex*, 319 NEW ENG. J. MED. 1573 (1988) (reporting improved cognition and significant reduction in intensity of symptomatic distress in recipients of AZT).

It is probably not possible to approve a drug faster than the FDA approved AZT. Although developed as a cancer drug in 1964, it was rarely used. In 1985, its antiviral possibilities were recognized at the NIH, and a Phase I trial was completed there and at Duke University. In early 1986, a Phase II trial was conducted at 12 medical centers, which resulted in the Fischl study discussed in *The Efficacy of AZT and The Toxicity of AZT*. Bartlett, *supra*, at 3051. While this study was being evaluated, the FDA permitted other physicians to prescribe AZT under a "compassionate use" treatment investigational new drug exemption. The Creagh-Kirk study, described in *Survival Experience*, followed these patients. *Survival Experience*, *supra*, at 3009. Phase III was essentially replaced with informal "monitoring" of patients receiving the drug. Although it was predicted that AZT would soon be replaced by a less toxic and more effective drug, this has not happened. "[AZT's] future appears bright due to the paucity of alternative antiviral agents with similar efficacy and acceptable toxicity . . ." Bartlett, *supra*, at 3052. See also Yarchoan, Mitsuya & Broder, *AIDS Therapies*, SCI. AM., Oct. 1988,

IV. SHOULD THE RULES FOR RESEARCH BE CHANGED WHEN THE DISEASE IS FATAL?

Randomized clinical trials (RCT) are the “gold standard” upon which experimental treatments are judged useful, worthless or dangerous.⁵⁸ John McKinlay has demonstrated that in the absence of an initial well-controlled clinical trial the typical innovation in modern medicine goes through seven stages: (1) promising report; (2) professional and organizational adoption; (3) public acceptance and state (third-party) endorsement; (4) standard procedure and observational reports; (5) randomized clinical trial; (6) professional denunciation; and (7) erosion

at 110 (key to new treatments for AIDS is finding antiretroviral drug with less toxicity than AZT).

Aerosolized pentamidine was given FDA approval for wider experimental use in early 1989 when it seemed likely that the drug was effective in prevention *Pneumocystis carinii* pneumonia in AIDS patients. The company which has exclusive rights to market the drug, however, has a checkered history with the FDA. LyphoMed was forced to close its Florida facility last year, and at its Chicago plant, where aerosolized pentamidine is manufactured, FDA inspectors found violations of “good manufacturing practice” so severe that the company voluntarily agreed to curtail production radically in May 1988 to try to bring the plant into compliance. In late 1988 the company was permitted to resume normal production. FDA’s Dr. Ellen Cooper says of putting sole responsibility for the manufacture of a life-saving drug into the hands of a company with this poor track record: “It’s not our job to say, ‘This is a B-minus drug company, so we’re going to wait and give approval to an A company.’” In fact, it appears that there is no communication between the drug approval arm of the FDA and its field inspectors of manufacturing plants. Mahar, *Pitiless Scourge*, *supra* note 56, at 24. LyphoMed is pricing the spray at \$100 a dose or \$1200 a year, compared to a French company that makes it available in England for \$28 a dose. *Id.* at 22.

The FDA has also decided to make ganciclovir, used for treating peripheral cytomegalovirus retinitis, available on a compassionate plea protocol. Staver, *FDA Ok's Compassionate Plea for AIDS Drug: Trials Continue*, *Am. Med. News*, Mar. 17, 1989, at 14, col. 1. *But see* Erice, Chou & Biron, *Progressive Disease Due to Ganciclovir-Resistant Cytomegalovirus in Immunocompromised Patients*, 320 *NEW ENG. J. MED.* 289 (1989).

58. *See, e.g.*, R. LEVINE, *ETHICS AND REGULATION OF CLINICAL RESEARCH* 211 (2d ed. 1986) (“At the time of this writing, the RCT is the gold standard for evaluating therapeutic efficacy.”). Clinical trials of drugs are loosely divided into three phases. Phase I trials are small and are intended to identify the drug’s toxicity in humans. Phase II trials continue the toxicity study, but are aimed primarily at establishing dosage ranges in a small population of humans. Only in Phase III is the drug actually tested for efficacy, usually using a large number of patients in a randomized clinical trial in which half get the investigational new drug, and half get either a placebo or the conventional treatment drug. The arm of the trial to which each patient is assigned is chosen at random. If neither the patient nor the physician know what drug the patient-subject is receiving, the trial is “double blind.” There is, of course, nothing inherently magical about the three phases, and equally valid methods of testing drugs for safety and efficacy could certainly be developed. For a further discussion of human testing, see *supra* note 54 and accompanying text.

and discreditation.⁵⁹ McKinlay has argued forcefully that to avoid the first four stages, and the last two, as well as the expense in terms of money and human misery that they generate, we must evaluate all newly proposed therapies at stage (5), the randomized clinical trial, before making the therapy generally available.⁶⁰ This view is widely endorsed in the scientific community.⁶¹ The trend has been to try to develop methods to evaluate surgery and other therapies by RCT as well, in an effort to improve the quality of care by eliminating costly therapies that provide no benefit. Although there are proposals for "community clinical trials"⁶²

59. McKinlay, *From "Promising Report" to "Standard Procedure": Seven Stages in the Career of a Medical Innovation*, 59 MILBANK MEMORIAL FUND Q. 374, 376-98 (1981).

60. *Id.* at 402. In a randomized clinical trial, a new drug is compared with a placebo or other drug, each being assigned at random to comparable patients. In a double blind study, neither the physician nor the patient knows who is getting the new drug and who is getting the placebo.

61. In the words of Samuel Broder, the New Director of the National Cancer Institute, commenting on AIDS patients taking unproven drugs: "People must remember that individual self-experimentation is extremely unlikely to yield meaningful results. . . . The only way to know whether or not a drug really works is to put it through a series of carefully controlled and scientifically sound clinical trials." Booth, *supra* note 43, at 1279. See also Boffey, *At Fulcrum of Conflict, Regulator of AIDS Drugs*, N.Y. Times, Aug. 19, 1988, at A13, col. 1 (noting conflict between scientists who seek well-controlled studies and AIDS sufferers who seek immediate access to drugs).

62. Halpert, *Community Facilities to Do AIDS Research*, Boston Globe, Nov. 23, 1988, at 12, col. 1. See also Abraham, *NIH Looks to Community Physicians for AIDS Research*, Am. Med. News, Dec. 9, 1988, at 3, col. 1 (researchers carrying out community-based clinical trials are more able to find subjects and can conduct less scientifically and technologically intense studies with wider spectrum of AIDS sufferers); Kolata, *Doctors and Patients Take AIDS Drug Trial Into Their Own Hands*, N.Y. Times, Mar. 15, 1988, at C3, col. 1 (community Research Initiative "believes it can identify useful drugs far more quickly than more formal university-based trials can").

The American Foundation for AIDS Research (AmFAR) publishes a regularly updated directory entitled "AIDS/HIV Experimental Treatment Directory" which, among other things, lists where various experimental treatments are available across the country. Page ii of the directory contains the following warning in bold print: "No representation, warranty or endorsement, expressed or implied, is made as to the validity or success of any of the treatments. This information is provided to you as source material only, has not been verified, and should not be relied upon as being accurate." The directory is available from AmFAR, 1515 Broadway, Suite 3601, New York, NY 10036-8901.

Larry Kramer expressed his rage to the gay community about RCTs, which he denotes as "double blind," in the following words:

Let's talk about double-blind studies that we're forced to endure. Did you know that double-blind studies were not created originally for terminal illnesses? I never knew that. Did you know that? How dare they, then, make us endure double-blind studies? They are ludicrously inhumane when two-thirds of this room could be dead in less than five years.

Double-blind studies are also exceptionally foolish, because PWAs

and for “adjustments” in the current management of RCTs,⁶³ there is little dispute that the RCT is the method most likely to produce valid results.⁶⁴

When Commissioner Young says that the FDA “has a heart as well as a mind,”⁶⁵ it is fair to ask whether the FDA’s role is to provide emotional support or scientific protection to the public. The FDA may see it as compassionate to provide access to un-

[persons with AIDS] lie to get the drugs. I’d lie. Wouldn’t you? If they told me what to say to get a promising treatment, I’d say it, whether it was true or not. I have friends who have forged their medical records, who have gone to medical libraries to learn the correct terminology to fill in the blanks. So all the results from all these double-blind studies aren’t going to tell anyone a thing. We’re willing to be guinea pigs, all of us. Give us the fucking drugs!

L. KRAMER, *supra* note 21, at 132 (1989).

Of course, new AIDS drugs should be compared to AZT in RCTs, not to a placebo, at least for those who can tolerate AZT.

63. Goyan, *Drug Regulation: Quo Vadis?*, 260 J. A.M.A. 3052, 3053 (1988). Jere Goyan, who is a former FDA Commissioner, argues that the changes the FDA has made to date amount primarily to speeding the procedure for drug approval, but not to making any changes in it. *Id.* Goyan challenges the entire procedure itself when he states that

our system needs much more than adjustment of the present process. It is time for us to consider the bases on which the current process was developed. In particular, we need to consider alternative study designs that allow the patient maximum hope for cure and the opportunity for some control over his or her destiny.

Id. But see Oates & Wood, *The Regulation of Discovery and Drug Development*, 320 NEW ENG. J. MED. 311, 312 (1989) (“The quality of evidence obtained in randomized controlled trials allows physicians and patients to make rational decisions about treatment. Real freedom of choice in therapy derives from evidence that permits an informed choice.”).

64. Nevertheless, it is this method of drug evaluation that is under attack. See, e.g., Mitchell & Steingrub, *The Changing Clinical Trials Scene: The Role of the IRB*, 10 I.R.B., July/Aug. 1988, at 1, 2 (controlled clinical trial is essential investigative tool).

The RCT is not totally without its critics. Some allege, for example, that it is too pure for actual medical practice, which does not follow precise inclusion rules nor precise dosages. Others think that, especially in the case of a universally fatal disease like AIDS, historical controls can be used instead of controls treated with either a placebo or AZT.

In a clinical trial using historical controls, control data are derived from the experience of the institution with the treatment of the disease in question accumulated before the introduction of the new therapy. Variants on this approach involve the use of literature controls (control data derived from publications on the outcomes of treatment with the best available standard therapy) and the use of control data developed in the conduct of other clinical trials. The strongest defense of the use of historical controls can be made when the disease in question has a uniformly lethal outcome when untreated and for which there is no effective therapy.

R. LEVINE, *supra* note 58, at 209-10.

65. Silver, *supra* note 56, at 3, col. 1.

proven remedies, but less than a decade ago it saw it as exploitative. Was the FDA right ten years ago, or is it right today?

I hope no one is surprised at this point that I think the FDA was correct on laetrile and should continue to insist on a scientifically valid randomized clinical trial before certifying drugs safe and effective. All consumer protection legislation is to some degree paternalistic; but in this case it is also realistic. FDA certification of the safety and efficacy of drugs recognizes that the public is in no position to judge the value or usefulness of many medications and that many are dangerous and have serious side effects (which is one reason we also license physicians and require some drugs be available only upon a physician's prescription). Furthermore, drug manufacturers have another social role: to create and sell new products. Their role is *not* consumer protection.⁶⁶

Libertarians and those with extreme views of individual autonomy, and even some free marketers, object to FDA regulation, equating "pursuit of quackery" with "life, liberty, and the pursuit of happiness."⁶⁷ True autonomy requires adequate and accurate information upon which to base decisions. This is simply impossible in the absence of responsible scientific study and properly designed clinical trials. It is appropriate to concentrate energies and resources in the time of an epidemic. It is also appropriate to assign AIDS drug testing a very high priority and to assure adequate governmental funding for the development and testing of drugs that might be effective.⁶⁸ It is also appropriate for the NIH and the FDA to work together more closely and to develop better dispute resolution systems when disagreements persist and delay

66. See J. YOUNG, *supra* note 45, at 410-12.

67. See Colen, *Laetrile Dispute Focuses Attention on Patients Rights*, Wash. Post, May 29, 1977, at 1, col. 6; see also Annas, *AIDS, Judges, and the Right to Medical Care*, HASTINGS CENTER REP., Aug./Sept. 1988, at 20, 21 ("There is no constitutional right to medical care, even to medical care that is lifesaving.").

68. NIH, for example, has blamed delays on staff shortages, though it might be their own fault that these staff shortages exist. See Boffey, *Official Blames Shortage of Staff For Delay in Testing AIDS Drugs*, N.Y. Times, Apr. 30, 1988, at 1, col. 2. But see Knox, *US is Stifling Development of AIDS Drugs, Senators Told*, Boston Globe, July 14, 1988, at 18, col. 1 (Commissioner Young said that his "agency could use at least 50 scientists above its fiscal 1989 complement to speed evaluation of AIDS drugs."); Kramer, *An Open Letter to Dr. Anthony Fauci*, Village Voice, May 31, 1988, at 18, col. 3 (problem is not staff shortages, but bureaucratic incompetence of Dr. Anthony Fauci, Director of National Institute of Allergy and Infectious Diseases). Regular review of FDA policies by outside experts is also reasonable to prevent the FDA from becoming "insular" and losing touch with new developments in testing methodologies. See Altman, *Mainstream Medicine Joins Growing Debate About Drug Approval*, N.Y. Times, Dec. 6, 1988, at C3, cols. 1, 4.

drug research.⁶⁹ But it is not appropriate or ultimately helpful to AIDS sufferers to rush inadequately tested drugs to market. The thalidomide episode taught us all that lesson,⁷⁰ and our brief experience with suramin should have reinforced it.⁷¹

The good news is that even with the “faith, hope and charity” rhetoric of the Commissioner, with the exception of permitting the importation of quack remedies for personal use, the FDA has actually stuck with its consumer protection role. Its two major rule innovations are designed primarily to speed the bureaucratic aspects of drug testing rather than to substantively change the rules for evaluating drugs. This is perfectly consistent with sound public policy. But it would not be in the public interest if the FDA adopted the anti-regulation agenda of the drug companies by relaxing its safety and efficacy standards.

The rhetoric is being turned up and is a repeat of the laetrile debate. For example, a *Wall Street Journal* editorial accused the FDA of killing people with its testing procedures, and called on the FDA to give in to the demands of dying patients rather than to insist on scientific soundness in experimentation and to let the “patients and their families” be involved in revamping the current system for drug approval:

Let defenders of the status quo explain to people with cancer, Alzheimer’s or AIDS why redundant efficacy testing, in which half the patients get a placebo, doesn’t constitute “killing” in the name of FDA-mandated medical statistics. . . .

. . . .

. . . AIDS patients have driven home to the U.S. medical and political establishment what enormous risks human beings in death’s grip will take to gain relief or respite.⁷²

69. See, e.g., *Scientific Necessity, Patient’s Rights*, U.S. NEWS & WORLD REP., Jan. 23, 1989, at 50-51 (some scientists feel FDA has relaxed rules too much while patient groups are clamoring for further relaxation of drug approval rules).

70. THE INSIGHT TEAM OF THE SUNDAY TIMES OF LONDON, *SUFFER THE CHILDREN: THE STORY OF THALIDOMIDE* (1979). Thalidomide was a tranquilizing pill that was said to be nontoxic, with no side effects and safe for pregnant women. The drug poisoned thousands of babies who were born with terrible handicaps. *Id.*

71. For a discussion of suramin, see *supra* note 48 and accompanying text.

72. *New Ideas for New Drugs*, Wall St. J., Dec. 28, 1988, at A6, cols. 1, 2. The drug approval process would be much more rational if the NIH, which produces drugs and performs clinical trials, and the FDA, which approves drugs, worked

What the *Journal* does not realize is that it has identified the *problem*—desperation—not the solution. Deregulation of the drug approval process cannot produce new drugs that do not exist. Of course, money can be made by exploiting the fear of death and desperation, and perhaps this is what the *Journal* would like to see. The continued insistence of Burroughs Wellcome to make AZT available only to those who can pay approximately \$8,000 a year for its use, long after the original justification (to recoup development costs) for this extraordinarily high price has been met, is a useful example of such financial exploitation.⁷³ No wonder that the American Public Health Association has petitioned the United States Department of Health and Human Services to require mechanisms be put into place to ensure that, if and when a drug more effective in combatting AIDS is developed at government institutions or with federal funding, it will be made available at the lowest possible price.⁷⁴ The quest for profit also threatens to inhibit scientific research and the sharing of data on experimental AIDS drugs, as well as to increase the likelihood that useless drugs will be hyped in press conferences rather than discussed at scientific meetings.⁷⁵ This trend is much more likely to adversely

together to set priorities. See Leary, *supra* note 26; Waldholz, *supra* note 55, at B3, col. 1.

73. See, e.g., *Forcing Poverty on AIDS Patients*, N.Y. Times, Aug. 30, 1988, at A18, cols. 1, 2 ("A drug company should not usually have to justify its profit, but AZT is a special case."). See also Lambert, *6,000 AIDS Patients Face Cutoff of Drug that May Prolong Lives*, N.Y. Times, Aug. 24, 1988, at A1, col. 1 (expiration of federal grant money allocated to helping certain AIDS patients gain access to AZT will jeopardize ability of 6,000 patients throughout country to obtain life-prolonging treatment).

Financial journals suggest that it is likely that Burroughs Wellcome recovered its approximately \$86 million in development costs involving AZT in the first year of its sales, and that even after a 20% price cut "the drug will continue to yield an appreciable profit." Mahar, *supra* note 56, at 20.

74. Boffey, *Federal Control Urged to Keep Costs Down on AIDS-Related Drugs*, N.Y. Times, Aug. 24, 1988, at B10, col. 1. Drug companies themselves will become increasingly difficult to regulate as the trend toward consolidation and merger in the \$127 billion global industry continues. Koenig & Lublin, *Global Drug Industry Appears to Be Headed for Big Consolidation*, Wall St. J., Apr. 13, 1989, at 1, col. 6.

75. See, e.g., Altman, *Cooperation vs. Competition*, N.Y. Times, Apr. 14, 1987, at C2, cols. 4, 5 ("[R]elease of data was often restricted by the commercial interests of not only for-profit biotechnology companies, with their patent concerns, but also some not-for-profit medical journals, which for competitive reasons may penalize researchers who disclose too many details before publication."); Foreman, *Secrecy in AIDS Research*, Boston Globe, Apr. 13, 1987, at 43, col. 4.

Wall Street, however, seems far less bullish on AIDS drugs in 1989 than it did just two years ago. Compare, for example, a front page *Wall Street Journal* article describing how AIDS has an appeal "reminiscent of the now-cooled ardor money men had for the microchip businesses of Silicon Valley. Venture capital-

affect AIDS sufferers than any FDA rule regarding clinical trials.

More importantly, drug companies are likely to continue to lobby Congress and the public to limit their liability for harm caused by dangerous drugs by eliminating the possibility of recovery for punitive damages when FDA standards have been followed, or by limiting liability for harm caused by vaccines.⁷⁶ AIDS activists may be tempted to join the drug companies and the free marketers on these moves as well, at least if the drug companies promise more work on AIDS drugs and vaccines in return. But just as drug approval standards should not be driven solely by the AIDS epidemic, so policies for compensating the victims of drug injuries should not be driven by the AIDS epidemic. We should not forget why we have rules for drug safety.⁷⁷

The distinction between experimentation and therapy is a powerfully useful and protective one that should not be undermined. The fact that there is no cure for a fatal disease does not make experimental drugs designed for it therapeutic, any more than a mechanical or baboon heart is therapeutic for someone with end stage heart disease.⁷⁸ Experimental drugs are not a consumer good appropriately governed by the free market. If consumer choice were the only relevant issue, even if it were limited to terminally ill consumers, the drug of choice among most dying intravenous drug users with AIDS would likely be heroin or other opiate derivatives such as morphine. These drugs *are* effective in relieving pain and anxiety in this population, and if delivered with clean needles in a medical setting, could also be safe. If we really wanted to make drugs a consumer good for the terminally ill, we should begin here. The fact that we do not indicates that the

ists are pouncing on all manner of AIDS enterprises, lavishing millions on private projects to diagnose, treat, prevent or cure the disease," Chase, *Venture Capitalists See Ways to Make Money in Combating AIDS*, Wall St. J., Sept. 28, 1987, at 1, col. 6, with a more recent article in *Barron's* that begins, "AIDS is a short . . . Wall Street has cooled on AIDS drugs over the past year . . . in part because a goodly number of [investors] have already been burned by the hype that inevitably accompanies any well-advertised scourge," Mahar, *Petiless Scourge*, *supra* note 56, at 6, col. 1-2.

76. There is at least some irony in the argument on the one hand that AIDS patients "have nothing to lose" and so cannot be hurt, and on the other that the possibility of being sued by injured patients is inhibiting the development of AIDS drugs. See also Mahoney, *The Courts Are Curbing Creativity*, N.Y. Times, Dec. 11, 1988, at F3, col. 1, col. 4 ("Additionally, good-faith compliance with up-to-date Government regulations like those of the F.D.A. should preclude the imposition of punitive damages.").

77. See, e.g., *supra* notes 44-55 and accompanying text.

78. See Annas, *supra* note 36.

political agenda at work in the AIDS context is not patient-centered.

Perhaps the fact that we do not make heroin available to terminally ill intravenous drug users is a way we have of punishing them for their illegal behavior. It is equally plausible that we care so little for the victims of AIDS that we do not care if they get hurt by quack remedies imported from abroad. It has also been suggested that although we do not accept active euthanasia and look with disapproval on even terminally ill patients who want physicians to end their lives, we nonetheless believe that it is perfectly acceptable for individuals to volunteer for medical experiments that could hasten their deaths:

Our quest for a formula that will banish death seems to make it acceptable to try questionable regimens on the aged and terminally ill Those who insist on using the dying as experimental subjects . . . see death as abnormal and dying patients as subhuman. We cast the terminally ill in modern rites of sacrifice, putting patients of experiments like the Jarvik heart through what one might see as torture in the hope of postponing the inevitable.⁷⁹

V. CONCLUSION

By making experimental drugs available to AIDS patients outside of organized clinical trials we are doing little, if anything, for AIDS patients. We are merely comforting ourselves with the illusion that something is being done to combat death—an illusion that is all the more satisfying because it does not call for any additional government funding. But we will pay a high price for this comfortable illusion if it is used as an excuse to abandon the distinction between experimentation and therapy and to transform the FDA from a consumer protection agency into a drug promotion agency.

The FDA has been the focus of much criticism for not producing a cure for AIDS. But this is not the FDA's responsibility. The FDA does not research, manufacture or test new drugs; it

79. Brauer, *The Promise that Failed*, N.Y. Times, Aug. 28, 1988, § 6 (Magazine), at 34, 76. It has also been persuasively suggested that as the costs of caring for AIDS patients increase, society will encourage them to opt for no care or a quick death "by seeming to leave individuals with no alternative to the indignities of their final days but to end them quickly." Schulman, *AIDS Discrimination: Its Nature, Meaning and Function*, 12 NOVA L. REV. 1113, 1140 (1988).

approves drugs as "safe and effective" that are made and tested by others who seek to market them in the United States. Its role is not to further the interests of drug companies, but to protect the public. It does this by insisting on strict standards in drug testing. Shortcuts that undermine these standards risk the health of all who later use a drug that has been too hastily approved.⁸⁰ The excuse that patients are dying without treatment and have "nothing to lose" will not do. Terminally ill patients can be harmed, misused and exploited. Realistic discussion of death and accurate education about the status of unproven AIDS drugs and the reason randomized clinical trials are needed is in order. It is not compassionate to make quack remedies easily available to those who can pay for them. True compassion demands that we allocate the money and staff necessary to do meaningful scientific research, and that when valid clinical trials demonstrate that a therapy is "safe and effective," we make it available to all who need it regardless of their ability to pay, not that we help supply dying patients with false promises and useless drugs.

80. The requirement of scientifically sound protocols and carefully controlled clinical trials applies to vaccines as well as drugs. See Mariner, *Why Clinical Trials of AIDS Vaccines Are Premature*, 79 AM. J. PUB. HEALTH 86, 86 (1989).

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